REMARKS/ARGUMENTS

Claims 35-37, 45 and 48-54 remain in this application and are not withdrawn.

Claim 35 is amended above to distinguish from the prior art cited, and the language of dependent claims 36, 37, 45 and 48 to 54 is amended above for consistency with new claim 35.

Currently claim 35 as amended above recites an oligomer or polymer of a saccharide bearing one or more pendant moieties that possess a group able to bind to a support, wherein each of the pendant moieties are linked to said saccharide via an amino linkage, and wherein the saccharide is fully functionalized.

Support for the claim as amended above can be found, for example, in the claims as originally filed (oligomer or polymer of a saccharide bearing one or more pendant moieties; fully functionalized), from page 14, line 18 to page 16, line 15 of the description (group able to bind to a support), and in page 10 of the description and in Example 1 (linked to said saccharide via an amino linkage). As such, applicants respectfully submit that no new matter is added.

Consideration and entry of this amendment are appropriate because the amendment places the application into condition for immediate allowance and does not necessitate additional searching.

Concerning the rejection of claims 35-37, 44, 45 and 48-54 under 35 U.S.C. 112

The Examiner has reapplied his rejection of claims 35-37, 44, 45 and 48-54 on the basis that there is no support for the use of the term "amino" in these claims. Reconsideration of this rejection is again requested.

As mentioned in the previous response, the reaction scheme found on page 10 of the description, which displays an oligomer or polymer according to an embodiment of the invention, clearly displays an amino linkage between the saccharide (β-cyclodextrin) and the electrophilic or nucleophilic moiety. While page 10 of the description names this linkage as an imino linkage, it is clear from the reactants used (-NH_2 and a tosylate group) that the only possible product from the reaction described is an amino linkage (-NH- or –NR-). In fact, none of the reaction schemes described in the description, including the examples, could lead to an imino (-N=) linkage.

Further support for the amino linkage is found, for example, in Example 1, where allylamine is reacted with mono-6-deoxy-6-β-cyclodextrin to give mono-6-N-allylamino-6-deoxy-β-cyclodextrin.

In light of the above, we submit that mention of "amino" linkages in the claims does not constitute an addition of new matter.

For consistency, the term "imino" on pages 3, 4 and 10 is corrected to read -- amino --.

Concerning the rejection of claims 35-37, 44, 45 and 48-54 under 35 U.S.C. 112

The Examiner has objected to the term "reactive" in the claims. The language of the claims is amended above to no longer refer to the term "reactive".

Concerning the rejection of claims 35-37, 44, 45 and 48-54 under 35 U.S.C. 102(b) and 103(a)

The Examiner has reapplied US Patent 6,017,458 (the '458 patent) against the above claims, saying that the reference anticipates and makes obvious the subject matter of these claims. Reconsideration of this rejection is requested in light of the amendments above.

In his objection, the Examiner states that the claims are anticipated by or, in the alternative, obvious over the '458 patent, and that any difference between the claims and the cited patent would reside in optimizing the elements of the '458 patent. Unfortunately, the Examiner has failed to define what is meant by "optimizing".

With regard to novelty, the claims as amended above are clearly not anticipated by the '458 patent as the cited reference fails to disclose an amino linkage between the oligomer or polymer of a saccharide (a cyclodextrin in the case of the '458 patent) and the support.

With regard to obviousness, as the Examiner has not cited any additional references in combination with the '458, we understand that the Examiner considers that all the elements of the claims would be known to a person skilled in the art in light of the teachings of the '458 patent and the common general knowledge in the field in question. However, there are no teachings in the '458 patent and the common general knowledge that would lead a person skilled in the art to replace urea linkages (as taught in the '458 patent) with the amino linkages found in the present claims. This assertion is supported by the fact that the reaction pathway necessary to achieve amino linkages is completely different than the reaction pathway used to make urea linkages. As such, there are no teachings in the '458 patent that would lead a person of skill in the art to the invention as claimed.

Concerning the rejections of claims 35-37, 44, 45 and 48-54 under 35 U.S.C. 103(a)

Applicant's response to the remaining rejections made by the Examiner have been combined below for clarity and succinctness.

The Examiner has rejected the claims, saying that they are obvious from either US Patent 5,639,824 to Okamoto (the '824 patent) or US Patent 5,198,429 to König *et al* (the '429 patent). The Examiner states that the claims differ only from these references in that they fail to recite:

a) fully functionalized;
b) silyl moieties; and
c) an amino linkage,

and that these differences would be considered to be obvious in light of US Patent Nos 6,017,458

to Ng et al. (the '458 patent), 5,104,547 to Cabrera et al. (the '547 patent), 4,298,500 to Abbott (the '500 patent) and 5,964,996 to Armstrong (the '996 patent). Differences a) and c) will be discussed below, and it will be shown that the teachings of the cited references do not, even in combination, disclose all the elements of the present claims.

Fully Functionalized

The Examiner states, on page 3 of the Action, that it would have been obvious to "cap" in Okamoto either because Ng and Cabrera disclose capping to block hydroxyl groups, or because Abbott discloses that capping the remaining available sites allows for separation of specific biomolecules. A similar statement, regarding the König reference, is found on page 5 of the Action.

However, the Examiner seems to have misconstrued the teachings of the passages referred to in each of the Ng, Cabrera and Abbott references. From a more careful reading of column 4, lines 1-7 of the Ng patent and of column 3, lines 48-55, of the Cabrera patent, it is clear that the end-capping reaction described does not refer to the functionalizing of the hydroxyl groups on the saccharide moieties, but of a functionalizing of the hydroxyl groups on the support member, which in both cases consists of a silica gel support. Similarly, while the language of column 8, lines 49-56, of the Abbott patent is not clear as to which groups are being "capped", it is clear from the language of the abstract:

> "...and "capping" other sterically available active sites on the support..."

that the groups being capped are those on the support.

As such, the passages relied upon by the Examiner to make his rejection of the claims of the present application do not disclose fully functionalized oligomers or polymers of a saccharide, but they disclose a post-reaction process where the reactive groups on a support are reacted with "capping" agents.

In the present invention, a pre-immobilisation functionalization of the saccharide is important, as it has been shown in the past that functionalization of cyclodextrin cannot be efficiently carried out after immobilization since it entails heterogeneous solid-liquid reactions. In fact, not all hydroxyl groups on cyclodextrin can be functionalized once the cyclodextrin has been immobilized. Therefore, the post-reaction processes taught in the passages relied upon by the Examiner would not be suitable, in combination with either of the Okamoto or the König et al. references, to render the present claims obvious.

Amino Linkages

On page 5 of the Action, the Examiner states that it would have been obvious to use an amine in the Okamoto reference (the '824 patent) because Armstrong (the '996 patent) discloses that ether and amines are interchangeable linking agents. Similar comments are made on page 7 of the Action with regard to the König reference (the '429 patent).

In the response to the previous Office Action, we brought to the Examiner's attention that macrocyclic antibiotics are complex molecules having a large number functional groups that can be utilised to perform linkages to a stable support, and that the strategies for attaching such molecules to a support do not automatically translate into sound strategies for linking pendant groups to an oligomer or polymer of a saccharide. In the re-application of his rejection in the present Action, the Examiner states that there is enough motivation to combine the teachings of the Armstrong reference with either of the Okamoto or the König reference. However, while there might or might not be such motivation to combine the Armstrong reference with either of the Okamoto or the König reference, the Examiner has failed to appreciate that the teachings found in the Armstrong reference are not applicable to the Okamoto or König references as cyclodextrins do not have the reactive groups necessary to perform the type of linkages accessible to macrocyclic antibodies, and that none of the cited references provide the teachings necessary to permit cyclodextrins to perform such linkages.

In order to attach an amino linkage to a cyclodextrin molecule, a reaction must occur, not at the oxygen atom of the hydroxyl group of the saccharide moiety, but at the carbon atom to which that oxygen atom is attached. There are no teachings in any of the cited references that would permit a person skilled in the art to perform the necessary reactions to obtain a saccharide moiety that is linked through an amino linkage. In the present application, the teachings necessary to obtain the amino linkage are provided, as it is taught that amine linkages are attached by displacement of an electrophilic leaving group (e.g. a tosylate group) attached to the saccharide moiety. There are no examples of such a process in any of the references cited. In all of the cited references that deal with immobilized cyclodextrin molecules, the reactions used to attach the cyclodextrin to a spacer or tether go through very different processes, and none of these processes would lead to the formation of amino linkages.

The teachings of the Armstrong reference are not applicable to the teachings of the Okamoto and König references, as no special reactions are required to obtain amino linkages with macrocyclic antibodies since most of these compounds already bear the amine groups required to obtain this linkage. In fact, all four of the macrocyclic antibodies exemplified in the Armstrong reference: Vancomycin, Streptomycin, Rifamycin B and 3,5 dimethylphenyl-derivitized vancomycin (Table 1) contain one or more amine groups suitable for obtaining amino linkages. The structures for Vancomycin, Streptomycin and Rifamycin B are shown in the accompanying Exhibit A. In the Armstrong reference, the amine moieties found on the antibodies were reacted with a linker, which linker is reported to be an isocyanate (-N=C=O) in the immobilisation procedure, and such a reaction follows a totally different chemistry from that reported in the present application.

Reconsideration of the Examiner's rejection is respectfully requested, as the statement relied upon by the Examiner in the Armstrong reference cannot be deemed to be applicable to the teachings of the Okamoto and König references.

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PATENT
Attorney Ref. No. 4810-62169-01/RJP

Information Disclosure Statement

Applicants acknowledge, with thanks, the Examiner's consideration of the Information Disclosure Statement that was filed on June 17, 2002.

The photocopy of the Form PTO 1449 that was signed and returned by the Examiner bears a notation: "No copy of AJ was filed."

Applicants respectfully disagree with that statement. According to the records of the undersigned, a copy of AJ (Li, et al., Cyclodextrins and Their Applications in Analytical Chemistry, *Chem. Rev.*, 1992, vol. 92, pp 1457-1470) accompanied the Information Disclosure Statement that was filed on June 17, 2002.

In any event, a copy of AJ is transmitted herewith along with a new Form PTO 1449 that lists that publication.

Applicants request that AJ be considered at this time and listed as a "reference cited" on the issued patent.

No fee should be required for this submission because a copy of AJ was filed on June 17, 2002.

Conclusion

Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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